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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/764,141	01/19/2001	Peter N. Devreotes	01107.00060	8190

22907 7590 05/02/2005

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EXAMINER
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CHANDRA, GYAN

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 05/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/764,141

Applicant(s)

DEVREOTES ET AL.

Examiner

Gyan Chandra

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 February 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11, 13-25, 56 and 77-93 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11, 13-25, 56 and 77-93 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 January 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                                                        |                                                                                         |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

## **DETAILED ACTION**

### **Status of Application, Amendments, and/or Claims**

The amendments to claims 79 – 86 and 91 have been made of record.

Claims 11, 13-25, 56, 77-93 are pending and are under examination.

### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 79-86, 91 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's arguments, see Remarks, filed 2/24/2005, with respect to claims 79-86 and 91 have been fully considered and are persuasive. The rejection of 35 USC § 112 of claims 79-86 and 91 has been withdrawn.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11, 14-19, 21, 22, 25 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyawaki et al. (Nature 388: 882-887, 1997) in view of Jin et al. (Mol. Biol. Cell 9:2949-2961, 1998).

The claimed invention is drawn to a functional heterotrimeric G protein comprising an  $\alpha$  subunit comprising a first amino acid sequence encoding a first fluorescent protein and a  $\beta$  subunit comprising a second amino acid sequence encoding a second fluorescent protein, wherein said first and second fluorescent proteins are capable of fluorescence resonance energy transfer (FRET).

Applicant argues that the heterotrimeric G protein is more complex than the calmodulin and M13 system taught by Miyawaki. Applicant argues that there is no reasonable expectation of success using the heterotrimeric G protein system, because more functional interactions are required.

Applicant's arguments filed 2/24/2005 have been fully considered but have not been found persuasive. Miyawaki teaches on page 882, column 2, that fusion proteins often preserve biochemical function and cellular localization. Miyawaki further teaches that FRET is a non-destructive method.

The teaching of Jin et al is set forth in the previous office action. Therefore, It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to make a fusion fluorescent protein to have a functional heterotrimeric G protein comprising an  $\alpha$ - subunit comprising a first fluorescent or luminescent protein and a  $\beta$  or  $\gamma$  subunit comprising a second fluorescent protein and

Art Unit: 1646

that the first and second fluorescent proteins are capable of FRET because Miyawaki et al teaches that the fusion of fluorescent protein usually preserve the biochemical functions and cellular localizations of the partner proteins. The person of ordinary skill in the art would have been motivated make the fusion proteins of heterotrimeric G proteins of Jin et al with a reasonable level of success because Miyawaki et al teach making a functional fusion protein with a fluorescent protein capable of FRET.

Claims 13, 77-86, 89, and 91-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyawaki et al. in view of Jin et al. as applied to claims 11, 14-19, 21, 22, 25 and 56, and further in view of Xu et al. (Proc. Natl. Acad. Sci. USA 96: 151-156, 1999).

The claimed invention is drawn to a heterotrimeric G protein wherein the first and second chimeric proteins are within 100 angstroms of each other, and where the first amino acid sequence encodes a first fluorescent or luminescent protein and the second amino acid sequence encodes a second fluorescent or bioluminescent protein, wherein the first and second fluorescent or luminescent proteins are capable of either FRET or luminescence resonance energy transfer (BRET).

Applicant argues that the heterotrimeric G protein is more complex than the calmodulin and M13 system taught by Miyawaki and that there is no reasonable expectation that many functional properties are retained with or without the modification of Xu.

Applicant's arguments have been fully considered but have not been found persuasive. The teachings of Miyawaki et al in combination with Jin et al are

Art Unit: 1646

summarized as set forth. Miyawaki teaches on page 882, column 2, that fusion proteins often preserve biochemical function and cellular localization. Miyawaki further teaches that FRET is a non-destructive method. The teachings of Xu et al. have been set forth in the previous office action.

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to attach the fluorescent donor and acceptor proteins taught by Miyawaki et al. in view of Jin et.al. within a distance of 100 angstroms. The person of ordinary skill in the art would have been motivated to use FRET and BRET interchangeably with a reasonable level of success because Xu et al teach that the optional distance for FRET is within 100 angstroms and the use of BRET over FRET offers advantages in photo-responsive cells.

Claims 20, 23-24, 87-88, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyawaki et al. in view of Jin et al. as applied to claims 11, 14-19, 21, 22, 25 and 56, and further in view of Medina et al. (J. Biol. Chem. 271: 24720-24727, 1996) and Wall et.al. (Cell 83:1047-1058, 1995).

Claims 20, 23-24, 87-88, and 90 are drawn to a functional heterotrimeric G protein comprising first and second fluorescent proteins capable of FRET, wherein the first amino acid sequence is within a helical domain of G protein  $\alpha$  subunit, and the second amino acid sequence is at the N-terminus of the  $\beta$  subunit.

Applicant argues that the heterotrimeric G protein is more complex than the calmodulin /M13 system taught by Miyawaki. Applicant argues that the heterotrimeric G

Art Unit: 1646

protein involves necessary protein-protein interactions and enzymatic activity that cannot be predicted from the teachings of calmodulin/M13 system.

Applicant's arguments have been fully considered but have not been found persuasive. The teachings of Miyawaki et al in combination with Jin et al are summarized as set forth. Miyawaki teaches that fusion proteins often preserve biochemical function and cellular localization. Miyawaki further teaches that FRET is a non-destructive method.

It would have been prima facie obvious to the person of ordinary skill in the art at the time the invention was made to attach a fluorescent donor protein such as cyan within the helical loop of the first protein as taught by Wall et al. and Medina et.al., and a fluorescent acceptor protein such as YFP to the N-terminus of the second protein for FRET as taught by Wall et al. One of ordinary skill of the art would have been motivated to make heterotrimeric G protein fusions because Miyawaki teaches that fusion proteins often preserve biochemical functions and FRET is a non-destructive method.

### ***Conclusion***

No Claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.



Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gyan Chandra whose telephone number is (571) 272-2922. The examiner can normally be reached on 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gyan Chandra  
AU 1646  
25 April 2005-04-25

  
JANET ANDRES  
PRIMARY EXAMINER